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Sedentary Behaviour in Rheumatoid Arthritis: Definition, measurement and implications for health

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Running head: Sedentary behaviour in RA

Abstract

Rheumatoid Arthritis (RA) is a chronic autoimmune disease characterised by high grade-inflammation, and associated with elevated cardiovascular risk, rheumatoid-cachexia and functional impairment. Sedentary behaviour is linked to heightened inflammation, and is highly pervasive in RA -likely as a result of compromised physical function and persistent fatigue. This high sedentarity may exacerbate the inflammatory process in RA, and hold relevance for disease-related outcomes. The aim of this narrative review is to provide an overview of the definition, measurement and health relevance of sedentary behaviour in the

context of RA. Contradictions are highlighted with regards to the manner in which sedentary behaviour is operationalized, and the significance of sedentary behaviour physiology for disease-outcomes in RA is outlined. The advantages and disadvantages of sedentary behaviour measurement approaches are also discussed. Against this background, we summarise studies that have reported sedentary behaviour and its health correlates in RA, and propose directions for future research.

Key Words: Sedentary Behaviour, Rheumatoid Arthritis, Inflammation, Sitting, Cachexia, Functional Disability, Cardiovascular Risk, Measurement validity, Accelerometer.

Key messages:

- Sedentary behaviour may exacerbate already heightened inflammation in RA and hold relevance for disease-related outcomes.
- Studies investigating sedentary behaviour in RA are limited by several methodological inconsistencies.
- Future studies should employ more rigorous and standardised methodologies to investigate sedentary behaviour in RA.

Introduction

Sedentary behaviour: definition and health relevance

The term sedentary behaviour (SB) - derived from the Latin term sedere, meaning to sit – and is often simply defined as too much sitting [1]. Until recently, a common misapprehension has been that SB merely reflects the absence of purposeful physical activity, defined as moderate activity of ≥ 3 metabolic equivalents (METS, 1 MET =oxygen consumed at rest i.e., 3.5 mL/kg-1.min-1; 3 METS reflects moderate paced walking). However, a lack of moderate intensity physical activity should be referred to, more accurately, as physical

inactivity [2]. Indeed, current thinking recognises that SB and physical inactivity are separate constructs, and can be operationalised as such.

In 2012, the Sedentary Behaviour Research Network (SBRN) defined SB as any waking behaviour characterised by activity of ≤1.5 METS and a sitting or reclining posture (e.g., television (TV) viewing, computer use, reading and driving) [2]. In contrast, physical inactivity is defined as insufficient/irregular engagement in moderate intensity activity of ≥3 METS towards recommended levels (i.e. 60 minutes/day for adults) [3]. Thus, physically inactive individuals can also be non-sedentary, where, in the absence of moderate intensity activity, they still engage in substantial amounts of light physical activity (i.e., 1.6 –2.9 METS) and spend little time sitting [3, 4]. Similarly, sedentary individuals can also be physically active, i.e., they spend large portions of the day sitting but engage in the recommended 60 minutes of MVPA each day (Figure 1).

This move towards a more consistent thinking with regards to the modern conceptualisation of sedentariness is born out of recent findings demonstrating that SB holds deleterious consequences for health independently of any beneficial effects of physical activity engagement [4-11]. In particular, there is evidence that implicates SB as a precursor of heightened systemic inflammation in both healthy and clinical populations, irrespective of levels of the anti-inflammatory effect of physical activity [8-11]. Indeed, there now exists a considerable amount of evidence demonstrating SB to be an independent risk factor for cardiovascular disease, the metabolic syndrome, sarcopenia and Type 2 diabetes, all of which have chronic systemic inflammation in common[9,10,12-16]. These independent health effects may result from differences in the acute and chronic physiological responses to sedentary behaviour vs. physical activity engagement[17]. Indeed, divergent cellular mechanisms are reported to underlie the decrease in lipoprotein lipase (LPL) activity that can occur in response to sedentary behaviour, compared to the increase in LPL observed during

physical activity. For example, LPL activity is ≥10-fold lower in red oxidative muscle fibres during sedentary behaviour, whereas a 2.5 fold increase in LPL activity is observed in white glycolytic muscle fibres after exercise. Similarly, LPL mRNA expression is increased in glycolytic muscles in response to physical activity, where no change is observed in mRNA expression following prolonged sitting [18-20]. Low levels of LPL are associated with increased levels of circulating triglycerides and decreased levels of high-density lipoprotein cholesterol (HDL-C)[18,21] - precursors of inflammation and contributors to the progression of cardio-metabolic and cardiovascular disease[22,23]. Thus, evidence points to the possibility that regulation of LPL activity might represent a key cellular mechanism underling the independent associations between sedentary behaviour, inflammation and adverse health outcomes.

Given that many individuals spend the largest proportion of the day being sedentary (e.g., 55–60% of waking hours) [24], reducing sitting time and sedentary behaviour change have become public health priorities for chronic disease prevention [1,3]. Consequently, an increasing number of large-scale cohort studies continue to advance our understanding of the determinants and health consequences of SB [8,25-27]. However, whilst research in this domain continues to grow exponentially from an epidemiological perspective, far less work has focussed on specific clinical cohorts.

Examining the relevance of SB for health outcomes in individuals for whom physical dysfunction may contribute towards increased sedentariness, particularly those for which inflammation comprises a substantial component of disease aetiology, is obviously important. A prime example of such a clinical population is individuals living with Rheumatoid Arthritis (RA) for whom inflammation is a chief contributor towards disease progression, functional disability and other adverse outcomes. Indeed, high levels of SB which may result from reduced functional ability and persistent fatigue, may perpetuate the adverse consequences of

an already heightened chronic inflammatory load, and further contribute towards the risk of cardiovascular disease, metabolic syndrome and inflammation-related cachexia.

Sedentary behaviour and Rheumatoid Arthritis

Sedentary-inflammation hypothesis

RA is a chronic autoimmune disease characterised by high-grade systemic and local inflammation, joint erosion, musculoskeletal deterioration and functional disability [28]. Common sequela of uncontrolled high inflammatory load in RA include joint pain and stiffness, fatigue, compromised psychological wellbeing (e.g. depression), reduced quality of life, high CVD risk, and cachexia, amongst others[29-38].

Since SB may relate to increased inflammation, it follows that it may hold implications for such RA features. This may lead to a vicious cycle, where compromised physical function, heightened fatigue and increased local disease activity, may increase sedentariness, which, in turn, may further exacerbate inflammation and contribute towards the severity of RA-related health outcomes[39]. Figure two describes the proposed pathways by which the cyclic relationship may occur, and underpins the need for more research into the implications of SB for people with RA.

In this article we consider sedentary behaviour specifically in the context of RA. We discuss current approaches utilised to measure it, summarise available data concerning its levels and health-related correlates in RA, highlight directions for future research, and provide recommendations for researchers pursuing work in this field.

Measurement of sedentary behaviour

The established definition of SB stipulates a consideration of both low energy expenditure ≤1.5 METS *AND* a sitting or reclining posture[2]. Thus, in order to accurately quantify levels of SB, measures should enable valid and reliable assessment of both the energy requirements of the activity and posture (i.e., whether sitting, reclining and standing).

Moreover, assessment methods should be validated for measurement of SB among the specific populations in which they are used. Assessment tools should also enable continuous data monitoring to permit the measurement of free-living SB, and include the ability to distinguish sleep from sedentary behaviours engaged in during waking hours. Finally, the ideal measure of SB would be low cost, easy to use by participants, and produce data that are easily analysed by researchers [40].

When deliberating the utility of different measurement approaches it is also important to appreciate the components of SB proposed to be relevant to health [41]. It is not only the total amount of sedentary time accumulated that may hold implications for health-related outcomes, but also the manner in which it is accumulated. Specifically, the number and length of sedentary bouts (uninterrupted sedentary periods), and the frequency of interruptions in sedentary time (sedentary breaks), have been linked to biomarkers of chronic disease in both clinical and non-clinical populations [8-10,26]. For example, prolonged sedentary bouts are adversely associated with C-reactive protein, triglycerides, HDL-C and plasma glucose [9,10,26], where more frequent sedentary breaks associate with beneficial changes to the levels of these biomarkers[8,9]. The importance of examining the contribution of specific behaviours to total sedentary time has also been underlined: certain sedentary behaviours, such as TV viewing, may be more detrimental to physical health than others [8]. Indeed, concurrent engagement in other unhealthy activities whilst participating in more passive (relative to mentally-active) sedentary activities has been reported to result in increased adiposity and poorer cardio-metabolic health (e.g., TV time snacking)[42]. Accordingly, the health-related constituents of SB have been conceptualised using the SITT formula as follows [43]; S_{ITT} – Sedentary behaviour frequency (number of bouts of certain duration)'; $_{S}I_{TT}$ – Interruptions (e.g., frequency of getting up during sedentary time); $_{SI}T_{T}$ – Time (duration of sedentary behaviours); $_{SIT}T$ – Type (mode or context of sedentary

behaviour). In the following sections, we provide information regarding the advantages and disadvantages of different SB measurement approaches which are currently used to assess one of more components of SITT (Tables 1 and 2), including a focus on the application and validity of measures used in RA studies (Table 3).

Current sedentary behaviour measurement methods

Overview

Tables 1 and 2 provide an overview of current sedentary behaviour measurement methods. The cost, and user-reported ease and burden of use for each are described (Table 1), as well as the ability of each measure to assess SITT components, and the reported validity and reliability of instruments (Table 2). The capability offered by objective measures to assess each facet of SB (sedentary energy expenditure and posture as per the SBRN definition) is also indicated (Table 2).

Self-report methods

Until recently, questionnaire-based methods have been most frequently used to investigate SB due to their low cost, low participant burden and ease of use[41] (Table 1). In general, questionnaires involve asking individuals to retrospectively estimate their total sitting Time ($_{SI}T_T$) and/or time spent in specific Types ($_{SIT}T$) of sitting behaviours (e.g., TV viewing). Diaries can also be used to gather information in this way, on the basis of time-referenced recall of behaviour (e.g., at the end of each day). However, the pervasive and varied nature of sedentary behaviours undertaken throughout the day, may limit the accuracy of recall. As a result, low validity and reliability are frequently observed with regards to retrospective self-report measurement methods (Table 2) [40,41,44].

To alleviate some of the problems associated with behavioural recall (e.g., social desirability [41]), diary-based methods that require repeated momentary time sampling (e.g., every 15 minutes), can be employed to gather real-time accounts of sedentary Time ($_{SI}T_T$) and

Type ($_{SIT}$T). A clear advantage of this approach (coined Ecological Momentary Assessment, EMA[45]) is that it enables assessment of behaviour as it occurs. However, the time taken to complete EMA, and the advanced statistical data processing needed to analyse the data collected, means this method results in moderate-to-high burden for both the participant and the researcher. Still, the contextual data collected via EMA may also provide valuable insight with regards to the social and physical environmental factors predictive of sedentary Time ($_{SI}T_T$) and Type ($_{SIT}$T) among different populations.

Objective methods

Addressing some of the limitations inherent in self-report, attention is shifting towards technological innovations in objective monitoring of SB, such as accelerometers - and to a lesser extent - posture sensors [40,41,46]. Accelerometers are small, lightweight devices, usually worn on the wrist, hip or upper arm, which enable data pertaining to movement patterns (e.g., trunk, wrist or ankle accelerations) to be recorded continuously over several days. Movement data recorded by devices are typically calibrated against energy expenditure assessed via indirect calorimetry in order to identify a sedentary threshold or cut-point at which accelerometer output (e.g., signal magnitude vector – gravity subtracted, or accelerometer activity counts [47]), can be interpreted to classify behaviours requiring ≤ 1.5 METs [48-50]. Continuous behaviour monitoring via accelerometry therefore enables measurement of Sedentary (S_{ITT}) bout frequency, sedentary time Interruptions (where activity counts cross the sedentary threshold) and sedentary Time ($_{SI}T_T$). Still, whilst offering a somewhat comprehensive assessment of SITT components, it is not clear which sedentary cut-point should be employed in studies of different populations. Currently, a threshold of <100 counts per minute (cpm) is almost universally used to represent sedentary time among diverse cohorts [41]. However, this cut-point – derived from calibration studies of healthy adults [39] – has not been validated among different groups for whom the energy

requirements of behaviour may vary substantially (e.g., older adults and patient groups)[51]. Indeed, where accelerometers have been used to measure physical activity engagement, it is common for researchers to develop and validate specific cut-points to classify different intensities of physical activity among different populations [52,53].

A further drawback of using accelerometers to quantify sedentary behaviour on the basis of accelerations/movement counts, is that non-sedentary activities requiring little movement may be misclassified as sedentary. For example, accelerometers may yield movement counts associated with sedentary activity (i.e.,<100cpm), during activities where energy expenditure is increased above sedentary levels (e.g., standing whilst lifting weights). Researchers have sought to overcome this limitation with the application of combined sensors that measure both movement and physiological response to activity (e.g., via heart rate, skin temperature)[54,55]. Still – even when combined with physiologic sensory ability – accelerometers lack the facility to accurately capture whether activities are undertaken whilst sitting/lying (i.e., sedentary) or standing (non-sedentary).

Posture sensors represent a recent advancement in sedentary behaviour research and are being used with increasing regularity in this field [46]. These devices are typically worn on the front of the thigh, and use accelerometer-derived information regarding thigh position (towards gravity) to determine posture classification (i.e.,time spent sitting/lying/standing). Available evidence suggests posture sensors, such as the activPAL, may offer a valid measure of Sedentary (S_{ITT}) bout frequency, sedentary time Interruptions ($_{S}I_{TT}$) and sedentary Time ($_{SI}T_{T}$) [56]. Still, it is important to recognise that with the application of posture sensors, sedentary energy expenditure is inferred indirectly based on the assumed energy cost of sitting/lying (i.e., ≤1.5 METS)[46]. Thus, when used in isolation, both postural sensors and accelerometers are both limited in the extent to which they can accurately measure sedentariness in alignment with the SBRN definition.

Multi-site monitors - such as the Intelligent Device Energy Expenditure and Activity monitor (IDEEA) and the Dynaport Activity Monitor (DAM) - may offer a novel solution to this challenge [57]. These devices use multi-site sensor attachment (e.g., on the waist and the thigh) to determine time spent lying, reclining, sitting, standing, and in locomotion, as well as the energy cost (METS, IDEEA) or movement intensity (meters/second^2, DAM) of activities [57,58]. However, the high cost of multi-site monitors combined with the high participant and researcher burden, means these instruments have not been employed extensively to study SB. Continued development of these approaches and subsequent validation work will help to confirm their effectiveness for measuring SB in different populations.

Application and validity of sedentary behaviour measurement methods in RA

Table 3 outlines the self-report methods and objective measurement methods currently employed to investigate sedentary behaviour in RA, and summarises results from studies that have examined measurement validity [56,59-61]. Preliminary work in this field suggests that overall, self-report instruments may not provide a valid assessment of time spent sedentary for people living with RA. Specifically, when compared to accelerometry, the Yale Physical Activity Survey (YPAS) and the International Physical Activity Questionnaire (IPAQ) are subject to substantial underreporting of sedentary time engagement in this patient group[59,60].

Considering objective measurement approaches, the activPAL has been found to offer an accurate assessment of time spent sitting, lying, standing and walking in people living with RA, when compared to direct observation. However, its validity for quantifying step count and the number of sedentary time interruptions has been queried (i.e., underestimation by 26% and 36%, respectively)[56]. The validity of the Sensewear Armband (SWA) has also been examined, with data indicating this device to underestimate sedentary time in RA (as computed using manufacturer-derived proprietary algorithms) when compared with energy

expenditure assessed via indirect calorimetry[61]. This underestimation was suggested to be due to the elevated resting energy expenditure observed in this patient population, relative to healthy adults in which the proprietary-SWA-algorithms tested were developed[61]. As such, these findings support the thesis that inaccuracies in sedentary time estimation may arise when studies in RA employ SB algorithms derived from calibration studies in healthy adults (e.g.,<100cpm –Table 3)[59,60,62,63].

Further perpetuating challenges surrounding SB measurement validity, discrepancies also arise with regards to the sedentary MET definition applied in RA studies. Specifically, whilst most studies in other populations have defined sedentary behaviour as ≤1.5 METS in line with the SBRN definition (based on <100cpm), recent research in RA has considered activities requiring ≤1 MET to represent sedentary activities[63,64]: it is therefore likely that common seated behaviours with an energy cost of between 1-1.5 METS (e.g., sitting and reading/typing/watching TV) are not captured in these studies[65-67]. Thus, the prevalence of sedentarity in RA may have been significantly underestimated in this work. Moreover, the application of inconsistent definitions of SB precludes comparisons across studies (of both RA and non-RA populations), hindering advancement in the understanding of SB epidemiology in this patient group.

Against this background, in the following sections, we describe the results of current research that has sought to investigate levels and health related correlates of SB in RA. We critically appraise the measurement approaches used, analytical decisions employed and how these may have impacted upon results reported and their interpretation.

Levels and health correlates of sedentary behaviour in RA

Levels of sedentary behaviour

Self-reported

Table 4 includes the results of the seven studies that have sought to measure levels of sedentary behaviour in RA using self-report [58-60,62-64,68-76]. Semanik and colleagues (2004) were among the first to investigate levels of SB in RA: using the YPAS, 48% of participants reported sitting for >6 hours/day [73]. More recently, Gilbert et al. (2015) – also using the YPAS – found that people with RA spend approximately 13 hours sitting/day, with 53% reporting >8 hours daily sitting time [60]. This is substantially higher than estimates of sedentary time observed in the majority of other self-report studies, which show 4-6 hours sitting/day in RA. There may be several reasons for such divergent results including different populations of RA patients studied, the time period during which studies were conducted, and the manner in which sitting time was estimated. For example, Yu et al. (2015) and Greene et al., (2006) relied on participant recall of total daily sitting time in their studies using the IPAQ and PADS respectively[59,72]. In contrast, Gilbert and colleagues (2015) calculated daily sitting time as: 24 hours, minus the sum of self-reported physical activity and sleep time[60]. In addition, we have proposed a cyclical relationship between inflammation, sedentariness, and further perpetuation of inflammation[39]. With this in mind, it is also important to consider that the higher estimates of sitting time observed in some studies might reflect elevated disease activity and/or a longer disease duration of the particular patient sample studied. Indeed, comparison of descriptive data indicates patients recruited by Gilbert et al., (2015) represented individuals with active disease (DAS-28 =6.44) and established RA (13.4 years)[60]. In contrast, studies reporting relatively lower estimates of sedentary time engagement included patients with less active disease (e.g., DAS-28 =2.6)[68], and shorter disease durations (e.g.,7.2 and 11 years)[59,68].

Despite evidence demonstrating specific sedentary behaviours to be particularly detrimental to health (e.g., TV viewing)[8], only two studies have distinguished between types of behaviour when assessing sedentary time accumulation in RA. Kramer et al., (2012) and Giles et al., (2008) reported TV viewing to occupy around 2 hours/day in people with RA[70,71].

Objectively assessed

Munneke and colleagues (2001) were the first to investigate the prevalence of objectively assessed sedentary behaviour in RA using the DAM (Table 4)[58]. Results indicated that over a 24-hour period, people with RA spent approximately 30.5% of time sitting and 42.1% lying. However, this study did not determine the MET costs associated with engagement in these activities. Rather, movement intensity was reported in units pertaining to speed and velocity (i.e., meters/second^2)[77] Analyses also did not distinguish waking SB from sleep time, which may have resulted in inflated SB estimates. The distinction between waking SB vs. sleep is certainly important to make[40]. That is, sleep is a vital restorative process and should not be counted as sedentary time when examining levels and health related concomitants of SB.

Following this initial work, it was over a decade later when other researchers begun to employ objective devices to estimate daily sedentary time in RA. In sum, these studies report between 9 and 19 hours sedentary time each day in people with RA (Table 4)[59,60,63,64,76]. These highly variable estimates are again most likely due to methodological discrepancies, including: the instrument used (e.g., GT3X vs, RT3 accelerometer vs. activPAL), the manner in which sedentary behaviour is defined and subsequently quantified (e.g.,<100cpm (equating to ≤1.5 METS), vs. ≤1 MET vs. time sitting/lying) and the data collection protocol (e.g., inclusion vs. exclusion of sleep time) (Table 4). However, a lack of detailed reporting with regards to sedentary

measurement/analysis protocols within studies, means the extent to which each of these factors may contribute towards differing sedentary time estimates in RA is difficult to establish[59,63,64,74,75].

Health correlates of sedentary behaviour in RA

Several recent studies have sought to examine health related correlates of sedentary behaviour for people living with RA, including associations with disease activity, physical function, muscle density, bone mass, and cardiovascular risk[59,63,70-72,75].

Disease activity

One study has examined the link between SB and RA-associated disease activity. In a cross-sectional study, Khoja et al., (2016) reported SB measured by the SWA, to be inversely related to disease activity score in a group of RA patients[63]. However, as with all cross-sectional studies, the causal direction of this association cannot be determined. Indeed, SB could represent both a consequence *and* a cause of increased disease activity in RA[78-80]. That is, early RA patients, and/or patients with controlled disease, may be better able to avoid excess sedentarity, relative to individuals with established RA and/or more active disease. Prioreschi et al., (2014) examined longitudinal associations between SB and several health outcomes in RA. They reported reductions in SB alongside declines in morning stiffness following DMARD therapy[75]. Such findings underline the need of carefully designed longitudinal studies that could address issues of directionality/causality of associations between inflammation, SB and different health outcomes in RA. In a similar vein, studies which compare the treatment efficacy of biologic therapies vs. more conventional synthetic DMARDs for concurrently attenuating disease activity *and* sedentary behaviour would offer an interesting research agenda.

Muscle density and functional disability

Greene et al., 2006, were the first to report negative consequences of SB in RA, demonstrating self-reported time spent sitting and lying to be associated with disability and pain[72]. Giles et al., (2008) later showed self-reported daily TV time to associate with deleterious consequences for functional ability in RA[71]. Specifically, this cross-sectional study revealed each hour of TV viewing per day, was associated with a 0.09 unit increase in functional disability. The subsequent findings of Kramer et al. (2012) showed that TV viewing was negatively related to total muscle density, while total muscle density was positively associated with functional ability. Thus suggesting decreased muscle density as a plausible mechanism underlying this association[70]. Findings such as these support the hypothesis of a sedentary-inflammation pathway in RA, and require further investigation: sedentary time may exacerbate inflammation-induced cachexia, a chief contributor towards reduced muscle density and associated declines in physical function in RA[81].

Bone mass

A recent study indicates SB may also be linked to lower bone mass in RA[62], holding implications for the development of osteopenia and subsequent osteoporosis. Prioreschi et al., (2015) reported patients with below average bone mass accrued 2 hours more accelerometer-assessed sedentary time each day (defined as <100cpm), than those with a normal bone mass[62]. The role of pro-inflammatory cytokines have been underlined in the development of osteoporosis in RA, with evidence for the efficacy of biologic therapies targeting inflammatory cytokines protecting against bone degradation[82]. Heightened local and systemic inflammation resulting from SB in RA, may therefore also contribute towards increased risk of osteoporosis in these patients.

Cardiovascular risk

Khoja et al. (2016) also reported detrimental associations of SB with a number of cardiovascular risk factors (i.e., body-mass-index, blood pressure, insulin resistance, cholesterol), as well as functional disability in RA[63]. However, given that sedentary behaviour was defined as activities ≤1 MET in this study, conclusions could not be drawn concerning the relevance of common sedentary behaviours requiring 1–1.5 METS (e.g., sitting and reading a book or newspaper) for CV risk and other specific outcomes. Nevertheless, Yu et al, (2015) reported in a recent cross-sectional study, that accelerometer-assessed SB (defined as <100cpm/≤1.5 METS) was negatively related to cardiorespiratory fitness in RA[59].

Future research recommendations and directions:

Research to date suggests high levels of sedentariness in people living with RA, which appears to be a significant contributor to their disease burden. However, to further our understanding of SB and its health consequences in this patient group, a great deal of work that employs a more rigorous approach specific to RA is required.

Considering the methodological shortcomings and inconsistencies among past SB research in RA, we propose a standardisation of methodology that could include the following components: first, the definition of SB as advocated by the SBRN should be employed consistently across studies; second, a combination of self-report (e.g., diaries) and objective measures of SB should be utilised to effectively examine the multiple constituents of SITT; third, objective devices ought to include where possible, a measure of both posture and energy expenditure; fourth, studies employing accelerometry should utilise validated cut-off points commensurate with activities characterised by ≤1.5 METS in people living with RA. Where possible disease-state specific cut-points (e.g.,early vs. established RA, active vs

inactive RA) should also be developed/validated to take into account inflammatory/metabolic variability observed within RA; fifth, SB accumulated during waking hours should be distinguished from time sleeping; sixth, there should be clarity about data collection protocols and analytical decisions employed (e.g., cut-off points/algorithms used).

On the basis of such recommendations, future research priorities in the field of SB in RA should include: first, validation of self-report instruments, and lab-based calibration/validation studies of objective devices for measurement of SB in RA – to include characterisation of the energy cost of common sedentary behaviours (i.e., activities undertaken whilst sitting and lying) and standing without ambulation; second, application of validated devices to enable accurate measurement of levels of SB in RA, including patterns of sedentary time accumulation as conceptualised by SITT; third, Studies designed specifically to examine the directionality (including bi-directionality) of links between SB, inflammation, physical and psychosocial health outcomes in RA – with particular emphasis on disease activity, rheumatoid cachexia, and cardiovascular risk profile. These should also examine whether associations with such health outcomes occur independently of levels of light, moderate and vigorous physical activity engagement.

We would like to emphasise that as yet, no studies have examined the implications of SB for psychological health and wellbeing in RA. This is perhaps due to the assumption that sedentary behaviour may contribute towards adverse health outcomes in these patients via physiological (e.g., inflammation) rather than psychological mechanisms. We therefore propose a parallel research agenda concentrated on investigating the contribution of sedentary behaviour to adverse psychological health outcomes in RA (e.g., depression, subjective vitality).

Conclusions

Sedentary behaviour has emerged as a major contributor to the risk of developing and the outcome of chronic disease independently of engagement in physical activity. Evidence indicates this is likely due to the heightened systemic inflammation resulting from high levels of sedentariness. The potential relevance of SB for health outcomes in RA is of obvious importance and notwithstanding methodological difficulties that can be resolved, should be investigated further. Such research may inform the development of effective sedentary behaviour change interventions, which are likely to improve health and enhance quality of life in people with RA.

Review criteria

This manuscripts cited in this review (Table 4) were found by searching the terms sedentary and rheumatoid arthritis in PubMed (up to January 2016). The search returned 55 manuscripts. An additional search with the terms sitting and rheumatoid arthritis returned a further 3 manuscripts (after cross-checking for duplicates). Abstracts and full texts were reviewed by the main author, to determine the definition and measurement of sedentary behaviour employed. Studies retained for inclusion in this review are those that defined sedentary behaviour as distinct from physical inactivity (i.e., a lack of purposeful/health enhancing physical activity above a moderate intensity), and operationalized sedentary behaviour in accordance with either low energy expenditure (i.e., $\leq$1.5 or $\leq$1 MET) or behaviours undertaken in a sitting or reclining posture. All procedures were in line with published guidelines for writing a narrative review [83].

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Reference List

(1) Owen N, Sparling PB, Healy GN, Dunstan DW, Matthews CE. Sedentary Behavior: Emerging Evidence for a New Health Risk. Mayo Clin Proc 2010;85:1138-1141.

(2) Sedentary Behaviour Research Network. Letter to the Editor: Standardized use of the terms 'sedentary' and 'sedentary behaviours'. Appl Physiol Nutr Metab 2012;37:540-542.

(3) Owen N, Healy GN, Matthews CE, Dunstan DW. Too Much Sitting: The Population-Health Science of Sedentary Behavior. Exerc Sport Sci Rev 2010;38:105-113.

(4) Hamilton MT, Healy GN, Dunstan DW, Zderic TW, Owen N. Too Little Exercise and Too Much Sitting: Inactivity Physiology and the Need for New Recommendations on Sedentary Behavior. Curr Cardiovasc Risk Rep 2008;2:292-298.

(5) Bankoski A, Harris TB, McClain JJ et al. Sedentary activity associated with metabolic syndrome independent of physical activity. Diabetes Care 2011;34:497-503.

(6) Rosenberg DE, Bellettiere J, Gardiner PA, Villarreal VN, Crist K, Kerr J. Independent Associations Between Sedentary Behaviors and Mental, Cognitive, Physical, and Functional Health Among Older Adults in Retirement Communities. J Gerontol A Biol Sci Med Sci 2016;71:78-83.

(7) Santos DA, Silva AM, Baptista F. et al. Sedentary behavior and physical activity are independently related to functional fitness in older adults. Exp Gerontol 2012;47:908-912.

(8) Healy GN, Matthews CE, Dunstan DW, Winkler EA, Owen N. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-2006. Eur Heart J 2011;32:590-597.

(9) Carson V, Wong SL, Winkler E, Healy GN, Colley RC, Tremblay MS. Patterns of sedentary time and cardiometabolic risk among Canadian adults. Prev Med 2014;65:23-27.

(10) de Rezende LF, Rey-López JP, Matsudo VKR, Luiz OdC. Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health 2014;14:333.

(11) Ford ES, Caspersen CJ. Sedentary behaviour and cardiovascular disease: a review of prospective studies. Int J Epidemiol 2012;41:1338-1353.

(12) Biswas A, Oh PI, Faulkner GE et al. Sedentary Time and Its Association With Risk for Disease Incidence, Mortality, and Hospitalization in Adults: A Systematic Review and Meta-analysis. Ann Int Med 2015;162:123-132.

(13) Ford ES, Kohl HW, Mokdad AH, Ajani UA. Sedentary behavior, physical activity, and the metabolic syndrome among U.S. adults. Obes Res 2005;13:608-614.

(14) Hamilton MT, Hamilton DG, Zderic TW. Sedentary behavior as a mediator of type 2 diabetes. Med Sport Sci 2014;60:11-26.

(15) Fitzgerald JD, Johnson L, Hire DG et al. Association of Objectively Measured Physical Activity With Cardiovascular Risk in Mobility-limited Older Adults. J Am Heart Assoc 2015;4:e001288.

(16) Hall DT, Ma JF, Marco SD, Gallouzi IE. Inducible nitric oxide synthase (iNOS) in muscle wasting syndrome, sarcopenia, and cachexia. Aging (Albany NY) 2011;3:702-715.

(17) Hamilton MT, Hamilton DG, Zderic TW. Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. *Diabetes* 2007;56.

(18) Bey L, Hamilton MT. Suppression of skeletal muscle lipoprotein lipase activity during physical inactivity: a molecular reason to maintain daily low-intensity activity. *J Physiol* 2003;551:673-682.

(19) Hamilton MT, Hamilton DG, Zderic TW. Exercise physiology versus inactivity physiology: an essential concept for understanding lipoprotein lipase regulation. *Exerc Sport Sci Rev* 2004;274:161-166.

(20) Hamilton MT, Etienne J, McClure WC, Pavey BS, Holloway AK. Role of local contractile activity and muscle fiber type on LPL regulation during exercise. *Am J Physiol* 1996;275 :E1016 –E1022.

(21) Goldberg IJ, Le NA, Ginsberg HN, Krauss RM, Lindgren FT. Lipoprotein metabolism during acute inhibition of lipoprotein lipase in the cynomolgus monkey. *J Clin Invest* 1988;81:561 –568.

(22) Toth PP. High-Density Lipoprotein and Cardiovascular Risk. *Circulation* 2004;109:1809.

(23) Wilson PWF, Grundy SM. The Metabolic Syndrome. *Circulation* 2003;(13):1537.

(24) Matthews CE, Chen KY, Freedson PS et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol 2008;167:875-881.

(25) Buman MP, Winkler EA, Kurka JM et al. Reallocating Time to Sleep, Sedentary Behaviors, or Active Behaviors: Associations With Cardiovascular Disease Risk Biomarkers, NHANES 2005-2006. Am J Epidemiol 2014;179:323-334.

(26) Healy GN, Wijndaele K, Dunstan DW et al. Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). Diabetes Care 2008;31:369-371.

(27) Biddle S J H, Cavill N, Ekelund U et al. Sedentary Behaviour and Obesity: Review of the Current Scientific Evidence. Department of Health 2010.

(28) American College of Rheumatology. 1987 Rheumatoid Arthritis Classification. 1987.

(29) Anderson KO, Bradley LA, Young LD, Mcdaniel LK, Wise CM. Rheumatoid-Arthritis - Review of Psychological-Factors Related to Etiology, Effects, and Treatment. Psychological Bulletin 1985;98:358-387.

(30) Douglas KMJ, Pace AV, Treharne GJ et al. Excess recurrent cardiac events in rheumatoid arthritis patients with acute coronary syndrome. Ann Rheum Dis 2006;65:348-353.

(31) Lee DM, Weinblatt ME. Rheumatoid arthritis. Lancet 2001;358:903-911.

(32) Panoulas VF, Metsios GS, Pace AV et al. Hypertension in rheumatoid arthritis. Rheumatology (Oxford) 2008;47:1286-1298.

(33) Nikolaus S, Bode C, Taal E, van de Laar MAFJ. Fatigue and Factors Related to Fatigue in Rheumatoid Arthritis: A Systematic Review. Arthritis Care Res 2013;65:1128-1146.

(34) Metsios GS, Stavropoulos-Kalinglou A, Koutedakis Y, Kitas G. Rheumatoid Cachexia: causes, significance and possible interventions. Hospital Chronicles 2006;1:20-26.

(35) Davis MC, Zautra AJ, Younger J, Motivala SJ, Attrep J, Irwin MR. Chronic Stress and Regulation of Cellular Markers of Inflammation in Rheumatoid Arthritis: Implications for Fatigue. Brain Behav Immun 2008;22:24-32.

(36) van Steenbergen HW, Tsonaka R, Huizinga TWJ, Boonen A, van der Helm-van Mil A. Fatigue in rheumatoid arthritis; a persistent problem: a large longitudinal study. RMD Open 2015;1:e000041.

(37) Kojima M, Kojima T, Suzuki S et al. Depression, inflammation, and pain in patients with rheumatoid arthritis. Arthritis Care Res 2009;61:1018-1024.

(38) Louati K, Berenbaum F. Fatigue in chronic inflammation - a link to pain pathways. Arthritis Res Ther 2015;17:254.

(39) Fenton SAM, Kitas GD. Rheumatoid arthritis: Sedentary behaviour in RA [mdash] a new research agenda. *Nat Rev Rheumatol* 2016;12:698-700.

(40) Healy GN, Clark BK, Winkler EA, Gardiner PA, Brown WJ, Matthews CE. Measurement of Adults' Sedentary Time in Population-Based Studies. Am J Prev Med 2011;41:216-227.

(41) Atkin AJ, Gorely T, Clemes SA et al. Methods of Measurement in epidemiology: Sedentary Behaviour. Int J Epidemiol 2012;41:1460-1471.

(42) Thorp AA, McNaughton SA, Owen N, Dunstan DW. Independent and joint associations of TV viewing time and snack food consumption with the metabolic syndrome and its components; a cross-sectional study in Australian adults. *Int J Behav Nutr Phys Act* 2013;10:96.

(43) Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N. Physiological and health implications of a sedentary lifestyle. Appl Physiol Nutr Metab 2010;35:725-740.

(44) Tudor-Locke CE, Myers AM. Challenges and Opportunities for Measuring Physical Activity in Sedentary Adults. Sports Medicine 2001;31:91-100.

(45) Shiffman S, Stone AA, Hufford MR. Ecological Momentary Assessment. Annu Rev Clin Psychol 2008;4:1-32.

(46) Edwardson CL, Winkler EAH, Bodicoat DH et al. Considerations when using the activPAL monitor in field-based research with adult populations. J Sport Health Sci 2016 [in press].

(47) Actigraphcorp.com. Actigraph White Paper: What is a Count? Pensacola, FL: Actigraph; 2008. Report No: 1.

(48) Freedson P, Bowles HR, Troiano R, Haskell W. Assessment of physical activity using werable monitors: recommendations for monitor calibration and use in the field. Med Sci Sports Exerc 2012;44(Suppl 1):S1-S4.

(49) Evenson KR, Wen F, Herring AH et al. Calibrating physical activity intensity for hip-worn accelerometry in women age 60 to 91-áyears: The Women's Health Initiative OPACH Calibration Study. Prev Med Rep 2015;2:750-756.

(50) Phillips LRS, Parfitt G, Rowlands AV. Calibration of the GENEA accelerometer for assessment of physical activity intensity in children. J Sci Med Sport 2013;16:124-128.

(51) Metsios GS, Stavrtpoulos-Kalinoglou A, Panoulas VF et al. New resting energy expenditure prediction equations for patients with rheumatoid arthritis. Rheumatology (Oxford) 2008;47:500-506.

(52) Puyau MR, Adolph AL, Vohra FA, Butte NF. Validation and calibration of physical activity monitors in children. Obes Res 2002;10:150-157.

(53) Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, Mcdowell M. Physical activity in the United States measured by accelerometer. Med Sci Sports Exerc 2008;40:181-188.

(54) Jakicic JM, Marcus M, Gallagher KI et al. Evaluation of the SenseWear Pro Armband to assess energy expenditure during exercise. Med Sci Sports Exerc 2004;36:897-904.

(55) Brage S, Brage N, Franks PW, Ekelund U, Wareham NJ. Reliability and validity of the combined heart rate and movement sensor Actiheart. Eur J Clin Nutr 2005;59:561-570.

(56) Larkin L, Nordgren B, Purtill H, Brand C, Fraser A, Kennedy N. Criterion Validity of the ActivPAL Activity Monitor for Sedentary and Physical Activity Patterns in People Who Have Rheumatoid Arthritis. Physical Therapy 2016;96:1093-1101.

(57) van Lummel RC, van der Slikke RMA, Uiterwaal M. An Objective Clinical Movement Analysis Concept for Outcome Research:"DynaPort". Orthopädie-Technik Quarterly, English edition 2002;1:6-15.

(58) Munneke M, de Jong Z, Zwinderman AH, Tijhuis GJ, Hazes JM, Vliet Vlieland TP. The value of a continuous ambulatory activity monitor to quantify the amount and intensity of daily activity in patients with rheumatoid arthritis. J Rheumatol 2001;28:745-750.

(59) Yu CA, Rouse PC, Veldhuijzen van Zanten JJ et al. Subjective and objective levels of physical activity and their association with cardiorespiratory fitness in rheumatoid arthritis patients. Arthritis Res Ther 2015;17:59.

(60) Gilbert AL, Lee J, Ma M et al. Comparison of Subjective and Objective Measures of Sedentary Behavior Using the Yale Physical Activity Survey and Accelerometry in Patients With Rheumatoid Arthritis. J Phys Act Health 2016;13:371-376.

(61) Tierney M, Fraser A, Purtill H, Kennedy N. Study to Determine the Criterion Validity of the SenseWear Armband as a Measure of Physical Activity in People With Rheumatoid Arthritis. Arthritis Care Res 2013;65:888-895.

(62) Prioreschi A, Makda MA, Tikly M, McVeigh JA. Habitual Physical Activity, Sedentary Behaviour and Bone Health in Rheumatoid Arthritis. Int J Sports Med 2015;36:1021-1026.

(63) Khoja SS, Almeida GJ, Chester Wasko M, Terhorst L, Piva SR. Association of Light-Intensity Physical Activity With Lower Cardiovascular Disease Risk Burden in Rheumatoid Arthritis. Arthritis Care Res 2016;68:424-431.

(64) Huffman KM, Pieper CF, Hall KS, St Clair EW, Kraus WE. Self-efficacy for exercise, more than disease-related factors, is associated with objectively assessed exercise time and sedentary behaviour in rheumatoid arthritis. Scand J Rheumatol 2015;44:106-110.

(65) Ainsworth BE, Haskell WL, Leon AS et al. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 1993;25:71-80.

(66) Ainsworth BE, Haskell WL, Whitt MC et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32:S498-504.

(67) Mansoubi M, Pearson N, Clemes SA et al. Energy expenditure during common sitting and standing tasks: examining the 1.5 MET definition of sedentary behaviour. BMC Public Health 2015;15:516.

(68) Loppenthin K, Esbensen BA, Ostergaard M et al. Physical activity and the association with fatigue and sleep in Danish patients with rheumatoid arthritis. Rheumatol Int 2015;35:1655-1664.

(69) Conigliaro P, Triggianese P, Ippolito F, Lucchetti R, Chimenti MS, Perricone R. Insights on the role of physical activity in patients with rheumatoid arthritis. Drug Dev Res 2014;75:S54-S56.

(70) Kramer HR, Fontaine KR, Bathon JM, Giles JT. Muscle Density in Rheumatoid Arthritis: Associations with Disease Features and Functional Outcomes. Arthritis Rheum 2012;64:2438-2450.

(71) Giles JT, Bartlett SJ, ANDERSEN RE, Fontaine KR, Bathon JM. Association of Body Composition With Disability in Rheumatoid Arthritis: Impact of Appendicular Fat and Lean Tissue Mass. Arthritis Rheum 2008;59:1407-1415.

(72) Greene BL, Haldeman GF, Kaminski A, Neal K, Lim SS, Conn DL. Factors Affecting Physical Activity Behavior in Urban Adults With Arthritis Who Are Predominantly African-American and Female. Physical Therapy 2006;86:510-519.

(73) Semanik P, Wilbur J, Sinacore J, Chang RW. Physical activity behavior in older women with rheumatoid arthritis. Arthritis Care Res 2004;51:246-252.

(74) Prioreschi A, Hodkinson B, Avidon I, Tikly M, McVeigh JA. The clinical utility of accelerometry in patients with rheumatoid arthritis. Rheumatology (Oxford) 2013;52:1721-1727.

(75) Prioreschi A, Hodkinson B, Tikly M, McVeigh JA. Changes in physical activity measured by accelerometry following initiation of DMARD therapy in rheumatoid arthritis. Rheumatology (Oxford) 2014;53:923-926.

(76) Paul L, Rafferty D, Marshall-McKenna R et al. Oxygen cost of walking, physical activity, and sedentary behaviours in rheumatoid arthritis. Scand J Rheumatol 2014;43:28-34.

(77) van Hees VT, van Lummel RC, Westerterp KR. Estimating Activity-related Energy Expenditure Under Sedentary Conditions Using a Tri-axial Seismic Accelerometer. Obesity 2009;17:1287-1292.

(78) Thomsen T, Beyer N, Aadahl M et al. Sedentary behaviour in patients with rheumatoid arthritis: A qualitative study. Int J Qual Stud Health Well-being 2015;10:10.

(79) Katz WA. Modern management of rheumatoid arthritis. Am J Med 1985;79:24-31.

(80) van Lankveld W, van't Pad Bosch P, van de Putte L, Näring G, van der Staak C. Disease-specific stressors in Rheumatoid Arthritis: Coping and well-being. Br J Rheumatol 1994;33:1067-1073.

(81) Summers GD, Metsios GS, Stavropoulos-Kalinoglou A, Kitas GD. Rheumatoid cachexia and cardiovascular disease. Nat Rev Rheumatol 2010;6:445-451.

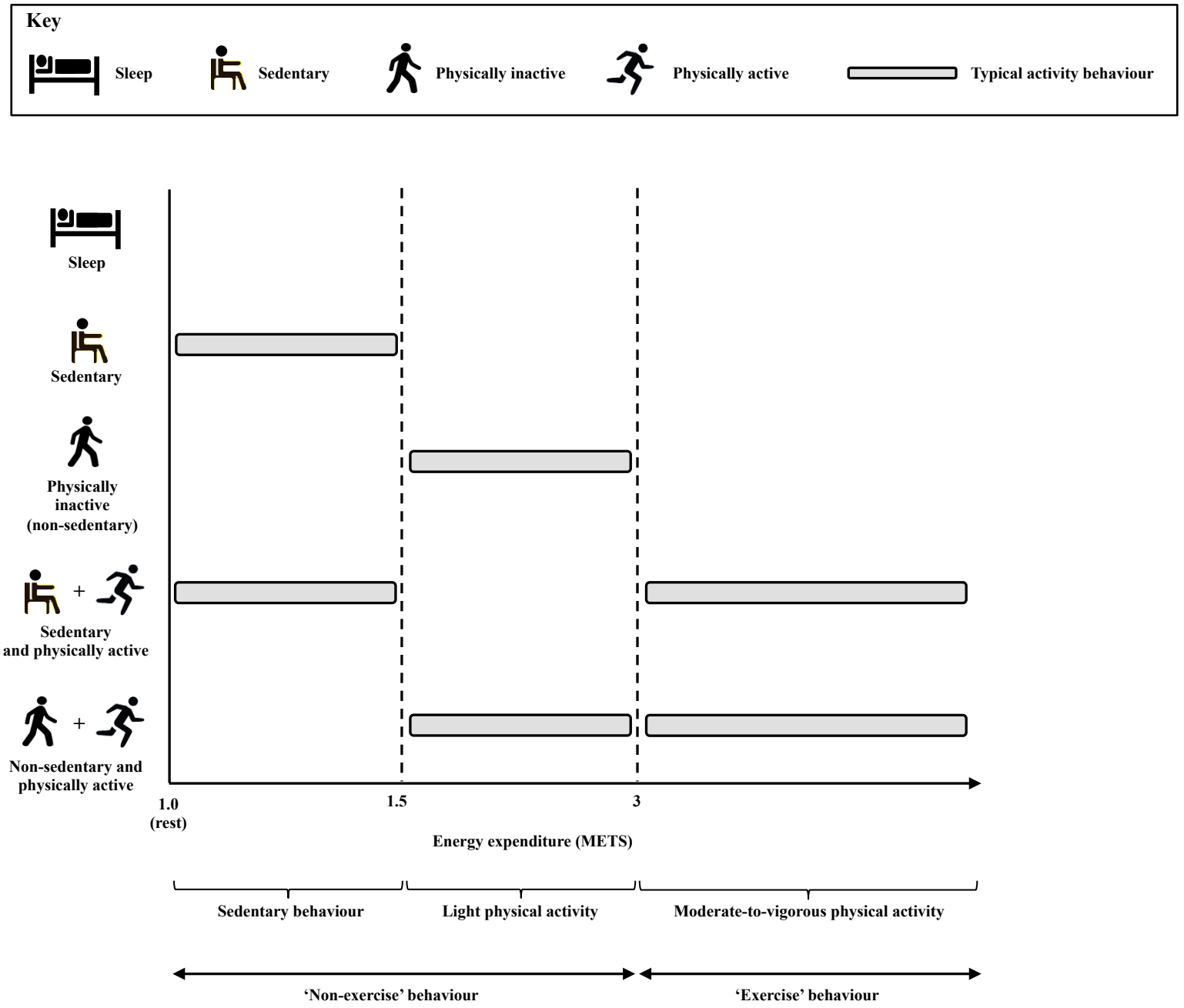
(82) Dimitroulas T, Nikas SN, Trontzas P, Kitas GD. Biologic therapies and systemic bone loss in rheumatoid arthritis. Autoimmunity Rev 2013;12:958-966.

(83) Gasparyan AY, Ayvazyan L, Blackmore H, Kitas GD. Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. Rheumatol Intl 2011;31:1409-1417.

Figure 1. Sedentary behaviour vs. physical inactivity
Four distinct behavioural profiles representing different levels of engagement in sedentary behaviour, light physical activity and moderate-to-vigorous physical activity. Physically activity: meeting guidelines for moderate-to-vigorous physical activity (children= 60 minutes x 7 days/week, adults= 30 minutes x 5 days/week). Physically inactive: absence of engagement in recommended levels of moderate-to-vigorous physical activity. Sedentary: the majority of waking time spent in activities ≤1.5 METS and a sitting or reclining posture.

Figure 2. Hypothesised sedentary behaviour-inflammation pathway in the context of RA

Proposed cyclic relationship between sedentary behaviour, local and systemic inflammation and the progression of RA outcomes. TNF-α: tumor necrosis factor alpha.


Key
Sleep
Sedentary
Physically inactive
Physically active
Typical activity behaviour
Sleep
Sedentary
Physically inactive (non-sedentary)
Sedentary and physically active
Non-sedentary and physically active
1.0 (rest)
1.5
3
Energy expenditure (METS)
Sedentary behaviour
Light physical activity
Moderate-to-vigorous physical activity
'Non-exercise' behaviour
'Exercise' behaviour

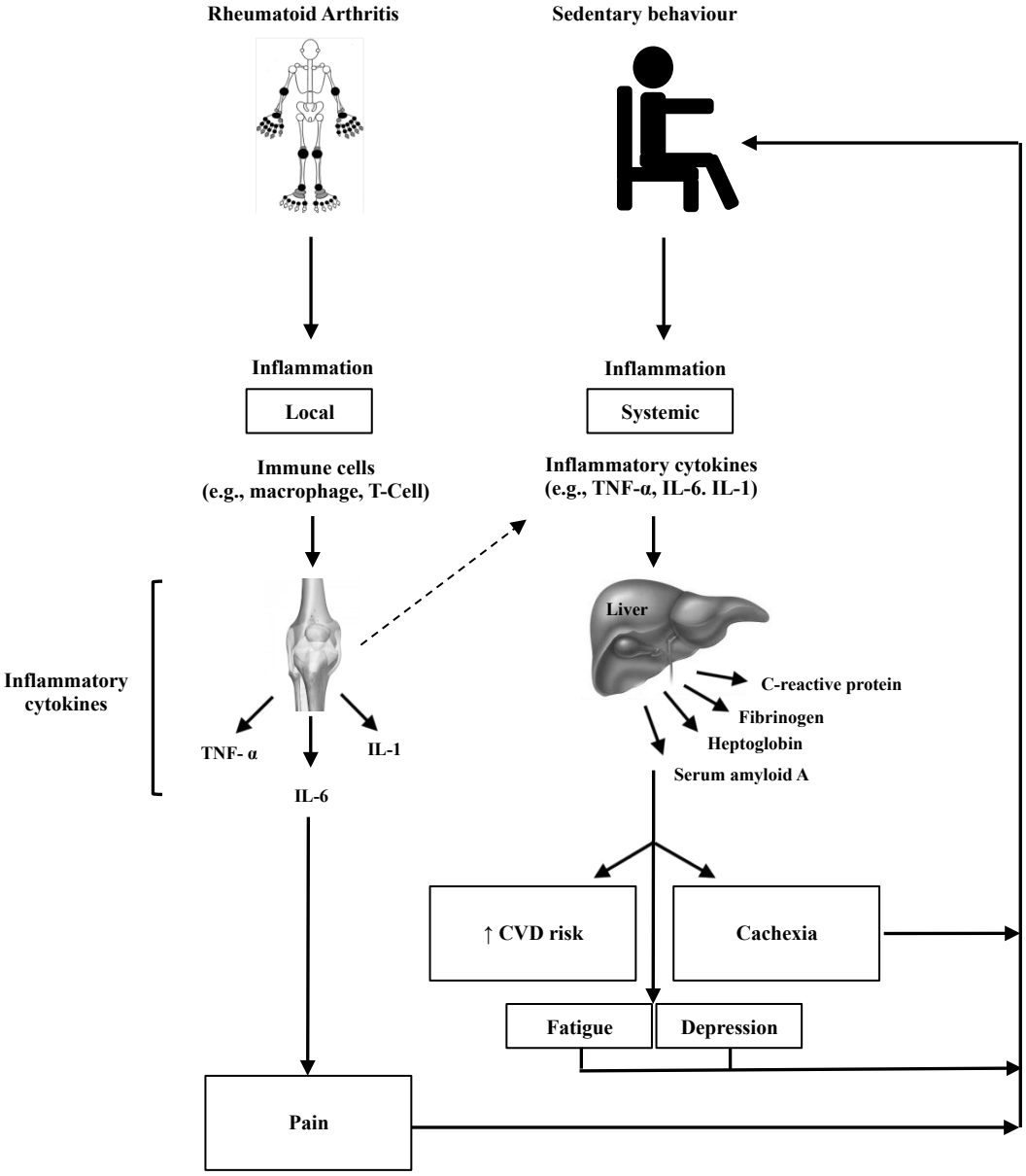

Rheumatoid Arthritis
Sedentary behaviour
Inflammation
Local
Inflammation
Systemic
Immune cells
(e.g., macrophage, T-Cell)
Inflammatory cytokines
(e.g., TNF-α, IL-6. IL-1)
Inflammatory
cytokines
TNF- α
IL-1
IL-6
Liver
C-reactive protein
Fibrinogen
Heptoglobin
Serum amyloid A
↑ CVD risk
Cachexia
Fatigue
Depression
Pain

Table 1. Existing sedentary behaviour measurement methods: cost, ease of use and burden

Measure			Perceived advantages/disadvantages			
Approach	**Type**	**Example**	**Cost**	**Ease of use**	**Participant burden**	**Researcher burden**
Subjective	Questionnaires	IPAQ, MOST	+	+ + +	+	+
	Diaries	Bouchard Physical Activity Record	+	+ +	+ +	+ +
Objective	Accelerometers	Actigraph	+ +	+ +	+ +	+ +
	Posture monitors	ActivPAL	+ +	++	+ +	+ +
	Combined sensors	Sensewear Armband	+ + +	+	+ +	+ + +
	Multi-site monitors	IDEEA monitor	+ + +	+	+ + +	+ + +

+: low; ++; moderate; +++: high; IPAQ: International Physical Activity Questionnaire; MOST: Measure of Older adults Sedentary Time; IDEEA: Intelligent Device for Energy Expenditure and Activity monitor.

Table 2: Reliability and validity of sedentary behaviour measurement methods

	Ability to measure SITT components				**Validity and reliability for measuring SITT component (in the general population)**			**Ability to (objectively) assess SB**	
Type of measure	**S_{ITT}**	**$_{S}I_{TT}$**	**$_{SI}T_{T}$**	**$_{SIT}T$**	**Reliability**	**Validity**	**Criterion standard used for validation**	**Sedentary activity METS**	**Posture**
Questionnaires	N	N	Y	N	+ +/+ + + (higher for TV viewing only)	+/+ + (higher for TV viewing only)	Accelerometer, Posture monitor		
Diaries	N	N	Y	Y	No detailed information	No detailed information	Accelerometer, Posture monitor		
Accelerometers	Y	Y	Y	N	+ +/+ + + (≥ 5 - 7 days of monitoring at ≥ 10 hours/day)	No consensus on cut-point to define sedentary time	Indirect calorimetry Posture monitor	Y	N
Posture monitors	Y	Y	Y	N	No detailed information	+ + + (limited studies at present)	Direct observation	N	Y
Combined sensors	Y	Y	Y	N	No detailed information	No detailed information	Indirect calorimetry (EE of sedentary activity)	Y	N
Multi-site monitors	Y	Y	Y	N	No detailed information	+ + +	Indirect calorimetry (EE of sedentary activity) Direct observation (posture)	Y	Y

Y: yes; N: no; +: low; ++: moderate; +++: high; S_{ITT}: Sedentary behaviour frequency; $_{S}I_{TT}$: interruptions; $_{SI}T_{T}$: Time; $_{SIT}T$: Type; IPAQ: International Physical Activity Questionnaire; IDEEA: Intelligent Device for Energy Expenditure and Activity monitor; EE: energy expenditure.

Table 3: Existing sedentary behaviour measurement methods: application and validity in RA

Type of measure	Measures used in RA	Validation study in RA	Number of studies	Criterion standard for validation	Conclusion
Questionnaires	YPAS	Y	2	Accelerometer (<100 cpm)	Underestimates sedentary Time
	LTPA Level Questionnaire	N	1	-----	-----
	PAS	N	1	-----	-----
	IPAQ	Y	1	Accelerometer (<100 cpm)	Underestimates sedentary Time
	7-day PARQ	N	2	----	----
	PADS	N	1	----	----
Diaries	None	N/A		----	----
Accelerometers	Actical	N	2	----	----
	Actigraph	N	3	----	----
	RT3	N	1	----	----
Posture monitors	ActivPAL	Y	1	Direct observation	Underestimates sedentary Interupptions Valid for measurement of Sedentary behaviour frequency and Time
Combined sensors	Sensewear armband	Y	1	EE assessed via indirect calorimetry	Underestimates sedentary Time
Multi-site monitors	DAM monitor	N	1		

Y: yes; N: no; YPAS: Yale Physical Activity Survey; LTPA: Leisure Time Physical Activity; PAS: Physical Activity Survey; IPAQ: International Physical Activity Questionnaire; PARQ: Physical Activity Recall Questionnaire; PADS: Physical Activity Disability Survey; DAM: Dynaport Activities of Daily Living (monitor); cpm: counts per minute; EE: energy expenditure.

Table 4: Studies using self-report and objective measures to determine levels of sedentary behaviour in RA

Study	**Sample size (N = RA patients)**	**Age, mean (SD)**	**Measurement of sedentary behaviour**	**Definition of sedentary behaviour**	**Variables derived**	**Levels of sedentary behaviour reported, mean ± SD**
Self-report studies						
Gilbert et al., 2015	N = 172	55.11 (13.91)	YPAS	Time spent sitting	% participants sitting for; <3, 3-6, 6-8 and >8 hours/day Daily sitting time continuous; (physical activity hours + sleep hours) – 24 hours	53% reported >8 hours sitting time per day 13 ± 2.59 hours/day sitting time (780 ± 155.40 min/day)
Løppenthin et al., 2015	N = 43	60 (range, 21–88)	LTPA Level Questionnaire PAS	Time spent primarily watching TV, reading books, other passive activities In your leisure time, how many hours/mins per day, do you watch TV, sit down and relax, read or listen to music etc.?	Sitting time (hours/day)	4 hours/day sitting time (range, 3-5 hours)
Yu et al., 2015	N = 68	55.00 (13.00)	IPAQ	Time spent sitting	Sitting time (minutes/day)	290 ± 159 min/day sitting time (4.83 ± 2.65 hours/day)
Kramer et al., 2012	N = 152	63.00 (8.00)	7-day PARQ	Duration of TV viewing	TV viewing (hours/day)	2 hours/day TV viewing (range, 1 – 3 hours)
Giles et al., 2008	N = 197	59.40 (8.70)	7-day PARQ	Duration of TV viewing	TV (hours/day)	2.3 ± 1.6 hours/day TV viewing
Greene et al., 2006	N = 52	61.00 (14.50)	PADS	Time spent sitting/lying down	Time spent sitting/lying (hours/day)	5.6 ± 3.4 hours/day sitting/lying
Seminak et al., 2004	N = 185		YPAS	(On average, how many hours/day are you sitting or lying down, not counting when you sleep at night)	% participants reporting; Sitting for > 6 hours/day Standing without movement for >3 hours/day	 48% reported sitting for >6 hours/day 75% reported standing without movement for >3 hours/day
Objective studies						
Gilbert et al., 2015	N = 172	55.11 (13.91)	GT3X accelerometer	<100 cpm	Sedentary time (hours/day)	9.86 ± 1.38 hours/day sedentary time (591.60 ± 82.80 min/day)

Prioreschi et al., 2015	N = 29	Low bone mass 57.00 (12.00) Normal bone mass 51.00 (10.00)	Actical accelerometer	≤ 100 cpm	Sedentary time (% waking hours/day) Sedentary time (min/hour)	Between 65 ± 4 and 73 ± 2 % waking hours/day sedentary 39.00 ± 6.00 to 44.00 ± 6.00 min/hour sedentary
Khoja et al.,2016	N = 98	58.00 (9.00)	Sensewear Armband	Activities <1 MET	Sedentary time (min/day) (including sleep time)	589 min/day sedentary time (SD not reported in text) (9.8 hours/day)
Yu et al., 2015	N = 68	55.00 (13.00)	GT3X accelerometer	(software algorithm not described)	Sedentary time (min/day) (including sleep time)	583.00 ± 98.00 min/day sedentary time (9.72 ± 1.63 hours/day)
Huffman et al., 2015	N = 41	55.00 (48, 64) (25th, 75th centile)	RT3 accelerometer	<100 cpm	Sedentary time (minutes/day) Sedentary time (% waking hours/day)	854.4 min/day sedentary time (SD not reported in text) (14.24 hours/day) 92.1 (range 89.2 – 95.3)% waking hours
Prioreschi et al., 2013	N = 50	48.00 (13.00)	Actical accelerometer	Activities <1 MET	Average counts spent in sedentary activity threshold (% waking hours/day)	71 ± 11% of waking time spent in sedentary activities
Prioreschi et al., 2014	N = 18	50.00 (14.00)	Actical accelerometer	(software algorithm not described)	Average number of activity counts spent in sedentary activity threshold per day	428 ± 124 counts in sedentary activity per day
Rafferty et al., 2014	N = 19	51.80 (12.50)	ActivPAL	Actical software algorithms used and not described	Time spent sitting/lying (hours/day) (including sleep time)	18.83 ± 1.72 hours/day spent sitting/lying (1,130 min/day)
Munneke et al., 2001	N = 41		DAM monitor	Actical software algorithms used and not described	Time spent sitting (including sleep time) and being; non-active active -with trunk movement Time spent lying (including sleep time)	 30.5 ± 9.1% of time in non-active sitting 2.0 ± 1.1% of time in active sitting 42.1 ± 8.8% of time lying

YPAS: Yale Physical Activity Survey; LTPA: Leisure Time Physical Activity; PAS: Physical Activity Survey; IPAQ: International Physical Activity Questionnaire; PARQ: Physical Activity Recall Questionnaire; PADS: Physical Activity Disability Survey; METS: metabolic equivalents; DAM: Dynaport Activities of Daily Living (monitor); MET: metabolic equivalent; cpm: counts per minute.